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GONADAL DOSE IN CANADA ARISING FROM THE CLINICAL USE OF UNSEALED RADIOACTIVE ISOTOPES

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Introduction

On first glance, the contribution to the gonadal dose from unsealed radio-nuclides should be very small indeed. The authors are unaware of any direct measurements having been made of this gonadal dose. A calculation by Clark[1] arrives at the figures of Table I for 1954 for the United States.

TABLE I

Isotope	Shipments from Oak Ridge[2]	Dose per year per person
I^{131}	557 curies	3 mr
P^{32}	153 curies	5 mr
	Total	8 mr

This figure is almost 9% of the natural background of 95 millirem per year as estimated by the Medical Research Council.[3]

The authors have calculated the gonadal dose in Canada for the year 1956. These calculations yield a gonadal dose much smaller than obtained by Clark for the United States.

Gonadal Dose from Unsealed Radio-Nuclides for Canada 1956

Table II summarizes the distribution of the isotopes of interest in Canada for the year 1956.

TABLE II

Distribution of Isotopes

Isotope	Shipped by A.E.C.L.*[4] to C. E. Frosst & Co.	Distributed by[5] C. E. Frosst & Co.
I^{131}	42.4 curies	31.3 curies
P^{32}	6.56	4.85
Au^{198}	24.9	24.9

*Calculated on the basis of shipments from April, 1956, to the end of January, 1957.

The dose to the gonads may arise from either beta particles or gamma rays or both. To calculate the dose from gamma emitters, one must know the location of the emitter, its distance from the gonads and the time of exposure. For a beta emitter, the problem is much more complex. The actual concentration of the beta emitter in the gonads and near the gonads (up to a distance equal to the range) must be known. Little information on this point is available so it has been assumed that, for a beta emitter, the dose to the gonads arises from the presence of the beta emitter in the blood stream and in the body tissue. It has been assumed that, except for certain organs which take up and hold a large amount of activity, all the activity which is not accounted for in these certain organs is distributed uniformly through body tissues and the blood stream. Calculations have been based upon the "Standard Man".[6]

Dose from Iodine^{131}

In the calculations we need make no distinction between diagnostic and therapeutic procedures from the point of view of gonadal dose. However, since the metabolism of the iodine depends upon the type of patient being treated, this will effect the gonadal dose calculations. The dose in a diagnostic procedure may be as high as 50 μc but probably averages 10-15 μc while the average dose for a hyperthyroid case is about 5 mc. These are in the ratio of about 1 to 500. Since there are probably 25 diagnostic cases to 1 therapy case, there will be about 20 times as much iodine used for therapy as for diagnosis. We will not be far in error then if we base our calculations on the assumption that *all* patients receiving iodine are suffering from hyperthyroidism and that the turnover of the iodine is typical of hyperthyroidism. We have assumed that in these cases, after 24 hours, 60% of the iodine is in the thyroid, 25% has been excreted through the bladder and 15% remains in the body uniformly distributed through the whole body mass[7,8]. The calculations which follow show that the main dose to the gonads arises from the iodine distributed through the body. The work of Hursh and Karr[9] suggests that

after 24 hours 13 to 20% of a test dose of iodine is uniformly distributed through the body whether it be given to hypo, hyper or euthyroid patients. Thus, regardless of the type of patient considered, we arrive at essentially the same gonadal dose.

The dose to the gonads arises from three sources of increasing importance as follows:

(a) Gamma rays from the radio-iodine deposited in the thyroid.

(b) Gamma rays from the radio-iodine being excreted via the bladder.

(c) Beta and gamma rays from the radio-iodine distributed uniformly throughout the remainder of the body tissues.

These will be considered in turn.

In the calculations which follow, the physical data has been taken from Table IB of Radiation Dosimetry, Hine and Brownell,[10] and all calculations are based on a given dose of 1 mc. We have further assumed an effective half life of 8.0 days, which will overestimate the dose.

(a) *Dose from iodine concentrated in the thyroid* (60% of the given dose).

The gamma ray dose rate constant for iodine is $\Gamma = 2.18$ r/hr per mc at 1 cm distance. Assuming the gonads are 60 cm from the thyroid and an attenuation factor of 64 (6 half value layers), the exposure dose to the gonads for 1 mc destroyed is

$$\frac{0.60 \times 2.18 \times 8.0 \times 1.44 \times 24}{64 \times (60)^2} = 0.00157 \text{ roentgens}$$

which corresponds to an absorbed dose in the gonads of 0.0015 rads.

(b) *Dose from iodine excreted through the bladder* (25% of the given dose).

To obtain the dose to the gonads from the gamma emitting iodine in the bladder, we require the emitted dose while the iodine is in the bladder. By assuming that the patient voids every 4 hours and that 25% of the given dose is excreted in the first two days with most of it in the first day, we obtain an emitted dose of 0.022 mc days. If we assume the bladder is 7 cm from the gonads and that there is 67% transmission through the tissue, then the exposure dose is

$$\frac{0.022 \times 24 \times 2.18}{(7)^2} \times 0.67 = 0.0157 \text{ roentgens}$$

which corresponds to an absorbed dose at the gonads of 0.015 rads.

(c) *Dose from the iodine distributed through the body tissues* (15%).

To obtain the dose to the gonads in this case, we must consider both the beta and gamma dose. We will assume that this 15% is uniformly distributed over the whole body and that it decays with a half life of 8.0 days. No distinction is made here between the amount present in the blood and the amount present in other body tissues.

The beta dose is easily determined from the mean energy of the beta particles, which for iodine is 0.187 Mev or by using the value $K = 110$ gm rads per microcurie destroyed.[10] This gives for the whole man an absorbed integral dose of $0.15 \times 110 \times 10^3 = 16.5 \times 10^3$ gm rads or an absorbed dose per gm of 0.236 rads to the standard man.

The gamma dose at a point P in the body due to the uniform distribution of the gamma emitter in the body will depend upon the position of P in the body. This exposure dose, $R\gamma p$ at the point P, is given by

$$R\gamma p^{(10)} = C.\ \rho.\ \Gamma.\ g_p \text{ r/hr}$$

where C is the concentration in millicuries per gm, ρ is the density of the body, Γ is the gamma ray dose rate constant (2.18) and g_p is a geometric factor. This geometric factor is plotted in Fig. 12, Chapter 17-111-A of Radiation Dosimetry[10] for points along the central axis of the human body. For the female ovaries, the g factor is 170 and is near the maximum value; for the male testes this factor is about 140. The average of these, 155, will be used in the calculations.

$$\text{Exposure dose rate} = \frac{(0.15)}{70{,}000} \times 2.18 \times 155 = 0.725 \times 10^{-3} \text{ r/hr}$$

which, for the complete decay of the isotope, gives an absorbed dose of *0.195 rads.*

A summary of these calculations are presented in Table III.

TABLE III

Dose to Gonads from 1 mc Given Dose of I^{131}

Organ	% Retained by Organ	Absorbed Dose to Gonads
Thyroid	60%	0.0015 rads
Bladder	25%	0.015 rads
Whole body	15%	
beta dose		0.236
Gamma dose		0.195
		0.45 rads

To obtain the significant gonadal dose, we must know what fraction of the patients receiving iodine are in the age group under 30 years. This is difficult to assess but experience in Canada indicates that less than 25% of the iodine is used in treating those under 30 years of age. Using this figure and assuming that only 75% of the iodine shipped by

Frosst is used, the significant gonadal dose is

$0.45 \times 0.25 \times 0.75 \times 31.3 \times 10^3 = 2640$ *rads.*

The total Canadian population under 30 years of age is 8.4 million so the gonadal dose per person per year is *0.314 mrad.*

From these calculations it is evident that the main contribution to the gonadal dose arises from the beta and gamma dose due to the uniform distribution of the isotope over the whole body. Unfortunately, there is little information on this point because patients are usually followed for only a day or two. In the above calculations, the dose has certainly been overestimated by using the physical half life for the effective one. On the other hand, the figure of 15% for the amount of isotope distributed over the body is not well established but it is not likely to be in error more than 30%. Marinelli and Hill[11] obtained a whole body dose of 1.08 equivalent roentgens per millicurie administered for a group of patients treated for thyroid carcinoma with large doses of iodine. Trunnell[12] obtained total doses of 0.65 equivalent roentgens to the ovaries and 0.33 to the testes per mc given dose. These compare well with the value 0.45 obtained here.

Phosphorus^{32}

Since P^{32} is a pure beta emitter we must consider the dose delivered to the gonads from the phosphorus carried to the gonads in the blood stream and from the phosphorus deposited in the gonads themselves. Turnover studies by Levenson et al[13] show that after 8 hours the whole blood contains about 0.053 mc of phosphorus per mc given dose. Unfortunately, there is no information on the concentration of the phosphorus in the gonads themselves. For this reason we shall take a more indirect approach by subtracting the quantities which we know can produce no gonadal dose from the given dose and then assume the remainder is distributed uniformly over the remaining parts of the standard man.

Osgood[14] and others state that when sodium radiophosphate is given by mouth, about 25% remains unabsorbed and is excreted from the body rapidly. This fraction cannot produce any dose to the gonads leaving 75% to be accounted for. Osgood states that for intravenous injections about 10% of the administered phosphorus is excreted through the kidneys in the first day. This leaves 0.68 mc to be considered. Low-Beer[15] states that 50% of this phosphorus is held in the "bony compartment" which includes liver, spleen and bone and the remainder, .34 mc, is found in soft tissue, muscle and blood where it decays with an effective half life of 9-10 days. The mass of the soft tissue compartment is about 60 Kg. We will assume then that the gonadal dose is due to 0.34 mc uniformly distributed over 60 Kg and decaying with an effective half life of 10 days. The mean energy of the beta particles from phosphorus is 0.69 Mev yielding a dose of 2.60 rads. It is likely that some of the organs considered in the 60 Kg take up a greater percentage of the phosphorus than the gonads so that this dose estimate is likely to be high rather than low. If we consider that the dose is due only to activity carried in the blood, we would arrive at a dose of about .60 rads which would be an underestimate.

In 1956, 4.85 curies were shipped by Frosst in Canada of which we have assumed 25% is lost by physical decay before being used. Again we must estimate the fraction of this isotope which is given to patients under 30 years of age. In Canada this figure is probably not more than 10%. Using these figures we obtain the annual gonadal dose to the population under 30 as

$2.60 \times 0.75 \times 0.10 \times 4.85 \times 10^3 = 950$ rads

Distributing this dose over 8.4 million people, we obtain a gonadal dose per person per year of 0.11 mrads due to P^{32}.

Gold^{198}

Radioactive gold is used almost exclusively in treating the peritoneal or pleural cavity and in Canada is confined to the treatment of patients over 30 years of age. Therefore, its contribution to the gonadal dose need not be considered.

Summary

A summary of these findings is given in Table IV.

TABLE IV
Summary of Results

Isotope	Dose to Gonads per mc dose	Dose per Person per year in 0-30 age group	Dose to Age 30	Dose to age 30 from natural background[3]
I^{131}	0.45 rad	0.31 mrad	9.30	
P^{32}	2.60 rad	0.11 mrad	3.30	
Au^{198}		0.00	0.00	
	Total	.42 mrad	12.6 mrad	2850 mrem

Table IV indicates that the dose to the gonads to age 30 from radio-isotopes in Canada for 1956 is less than 0.5% of that due to natural background. The calculations are based upon a number of questionable assumptions but in all cases the dose has been overestimated rather than underestimated. They are not in agreement with those of Clark who finds the dose is 9% of background for the U.S.A. Since the contribution of ingested isotopes to the gonadal dose is very small, it is doubtful if the problem warrants much detailed study. However, if it does, the study might well proceed along the following lines.

To improve the accuracy of these calculations:

(1) The age distribution of those receiving iodine and phosphorus should be obtained.

(2) The distribution and effective half life of iodine and phosphorus in organs other than the critical organs for periods up to 3 weeks should be determined.

Information for (2) could be obtained by following the excretion, the blood levels, thyroid levels over periods up to three weeks. As an alternative and in conjunction with this, the total body gamma activity could be obtained using a large scintillation counter in a well shielded room. Some information concerning the gonadal dose might be obtainable using a small photomultiplier and crystal positioned in the vagina or next the scrotum. However, because much of the dose is due to beta rays, there would be considerable difficulty in interpreting such results.

Acknowledgments

The authors take pleasure in acknowledging the help received through discussions with Dr. W. Paul, Dr. R. Volpe and Miss Amy Britton of the University of Toronto.

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RADIOLOGIC STUDY OF PHYSIOLOGIC KNOCK KNEE IN CHILDHOOD*

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There is a large surgical literature on the subject of knock knee in childhood, but the published literature on the subject does not include any adequate radiologic study. In recent years it has been made increasingly clear that most cases of knock knee in childhood are physiologic variations of normal and that almost all of them undergo spontaneous correction.[3,8] Knock knee caused by disease usually has clinical and radiologic features that allow distinction from the physiologic cases.

Definition

Knock knee (genu valgum) is defined as any malleolar separation when the medial surfaces of the knee just touch with the lower extremities in the anatomic position, i.e. with the patella and the great toe pointing directly anteriorly. A very useful classification with division into physiologic and pathologic forms of knock knee was given by Stelling and Meyer,[13] and a modified form of this classification is shown in Table I. Stelling and Meyer discuss both bowleg and knock knee, and from their classification we have removed those cases in which bowleg predominates, and we have added some unusual causes of knock knee, not included in their classification.

Natural History

Price[11] gave a clear account of the postural changes in the lower extremities of the growing child. In the first two years of life, there is a "varoid phase" (bowing). The lower extremities show an outward curve; at their lower ends (lower legs and ankles) there is an inward twist ("torsion"). These features are present at birth and disappear by approximately 2 years of age. The bowing appears to be chiefly in the bones, rather than at the knee joint. The toes are normally directed medially, approximately 15° when the child begins to walk, and there is about ½" separation between the medial surfaces of the knees. This physiologic bowing of the lower extremities can, in some infants, become greatly exaggerated ("non-rachitic bowing of the lower extremities"), and there is ample documentation of the spontaneous return to "normal" alignment in such children with markedly bowed lower extremities.

After 2 years of age, there is a "valgoid phase" of development, due to straightening of the tibiae and presumably to laxity of the knee joint ligaments.[2] These changes are most marked at 4 years, when malleolar separation may normally be 2" lying or 2½" standing. By 6 years the valgoid phase is usually ended.

Physiologic knock knee is rare before 2 and most marked at age 3 to 3½ years on the average. Malleolar separation of up to 4 or 5" may be seen in some children and even these cases straighten spontaneously. In some cases, there is said to be a familial tendency.

Case Histories

L. L. Case #1. Age 5 years. Female. This child was referred for x-ray examination at age 2½, because of bilateral genu valgum, more marked on the left than on the right. AP projections of the lower extremities showed the genu valgum and no other abnormality, with the exception of slight lateral bowing of the lower tibiae. No treatment was given. The child was recalled at age 5. The lower extremities were straight, and there were no related symptoms or signs.

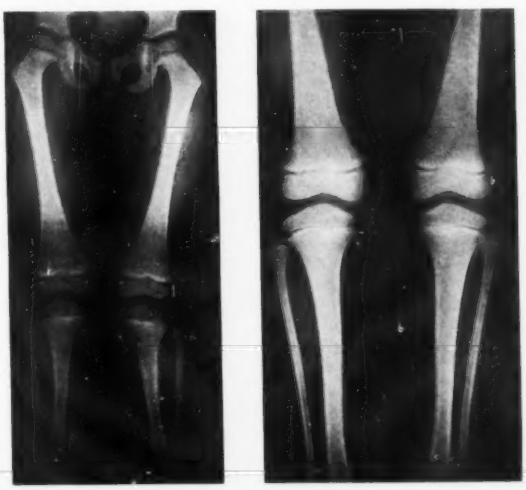

Fig. 1. Case 1.
A. Age 2½ B. Age 5

Presented at Annual Meeting, The Canadian Association of Radiologists, January 12 - 15, 1958, London, Ontario.

F. S. Case #2. Age 5½ years. Female. This child was first seen at age 4, with bilateral genu valgum, much more marked on the right than on the left. No treatment was given and the child was recalled for follow-up examination only, at age 5½. At that time the lower extremities were straight and there were no signs or symptoms related to them.

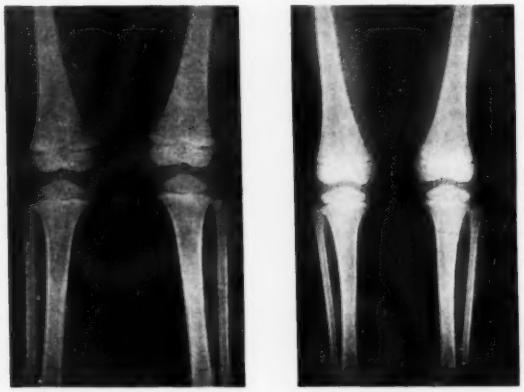

Fig. 2. Case 2.

A. Age 4 B. Age 5½

R. C. Case #4. Age 9 years. Male. This child was first x-rayed at age 5 years, when running was made difficult as the knees knocked together. There were no other symptoms. AP projections of the lower extremities showed moderate bilateral genu valgum and no other abnormality. No treatment was given. When recalled at age 9 years, the physical and x-ray findings were those of normal lower extremities. There were no symptoms. Osteotomy had been seriously considered at one time to correct this child's deformity.

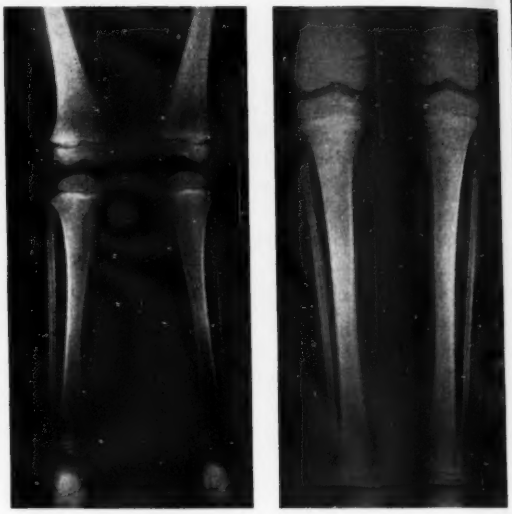

Fig. 4. Case 4.

A. Age 5 B. Age 9

J. R. Case #3. Age 6 years. Male. This child was first referred at the age of 3 years for bilateral genu valgum. The AP projections showed this and no other abnormality. 3/16" inner heel lifts on both sides were prescribed to protect the feet. No other treatment was given. The child was recalled for re-examination at age 6 years. The lower limbs were straight and there were no signs or symptoms related to them. The x-ray appearance was normal.

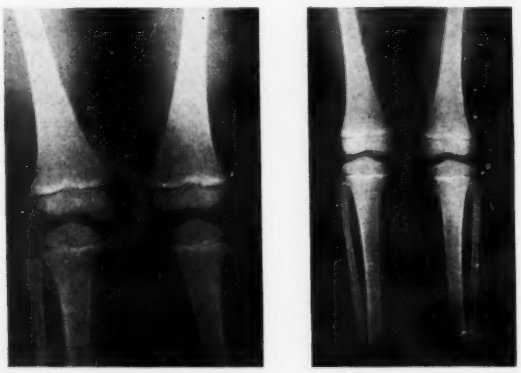

Fig. 3. Case 3.

A. Age 3 B. Age 6

P. H. Case #5. Age 4½ years. Male. This child was first x-rayed at age 3 years, because of bilateral knock knee. The x-rays showed the genu valgum and no other abnormality. The child was symptom-free and was treated with medial heel lifts only. On recall for re-assessment at age 4½ years, the knock knee was less severe and the parents had noted a marked improvement in gait.

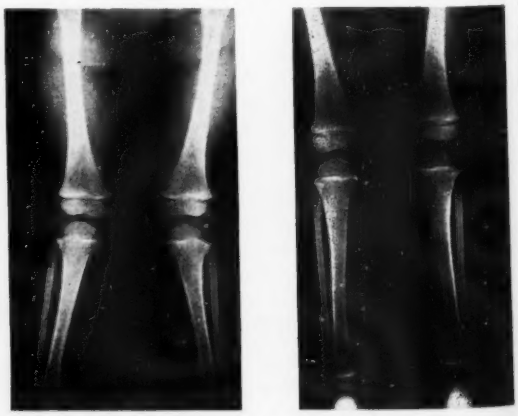

Fig. 5(a). Case 5.

A. Age 3 B. Age 4½

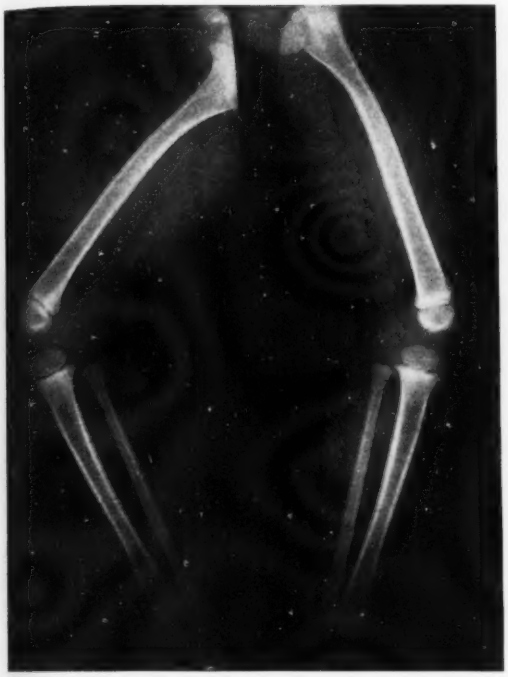

Fig. 5(b) Case 5.
C. Lateral, Age 3

D. C. Case #6. Age 6 years. Male. On routine examination by a pediatrician this child was found to have bilateral knock knee at age four. The parents had not noticed the deformity. On further questioning the child, there was a complaint of mild and occasional pain on the medial aspect of each lower thigh and knee. Clinical and radiologic examination showed bilateral genu valgum and no other abnormality. No therapy was given. Follow-up examination at the age of 6 years showed a symptom-free child without clinical or x-ray evidence of abnormality of either lower extremity.

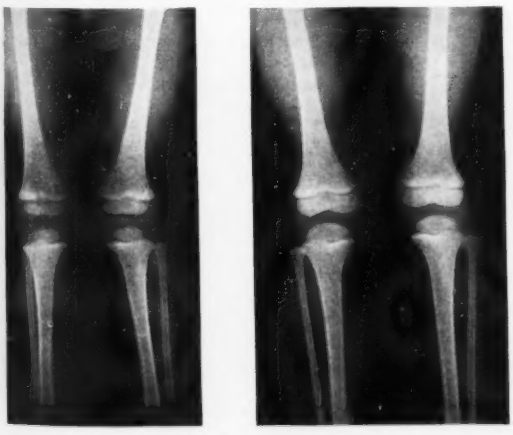

Fig. 6. Case 6.
A. Age 4 B. Age 6

A. P. Case #7. Age 5 years. Male. At the age of 2½ years this child was seen by an orthopedic surgeon because of complaint of leg pain and the parents' concern over knock knees. Knock knee was demonstrated radiologically and it involved the left more than the right side. The left lower extremity was 1" shorter than the right on clinical measurement. This was demonstrated by x-ray to be due to pelvic tilt. Heel and sole lifts for the left side were prescribed. No other therapy was used. The final clinical and radiological examination showed complete return to normal.

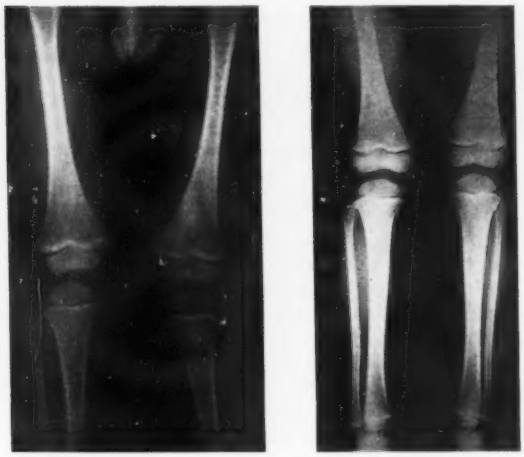

Fig. 7. Case 7.
A. Age 2½ B. Age 5

Comment

This group of 7 cases show the typical changes of physiologic knock knee. In each case the first x-ray and clinical examination showed genu valgum, always bilateral, but sometimes (particularly in Case #2) more marked on one side than on the other. The final examination in each case showed return to normal. Four of these cases received no therapy at all; the others had small wedges or lifts used on one or both sides.

The present study does not permit us to draw any conclusions about the value or otherwise of wedges or lifts used in the shoes. It is evident from the literature on the subject that for many years various forms of corrective device have been felt to be desirable or essential in the treatment of knock knee in children,[1,6,10,12] and among these, shoe lifts and wedges have been used. More recently, the increasing recognition of the tendency for the apparent deformity to correct itself spontaneously has been paralleled by de-emphasis on treatment.[8] Some authors still recommend these devices. Others feel that they are unnecessary or that while they do not alter the genu valgum, they may be of value in protecting the soft tissues of

the feet from injury caused by the altered weight-bearing stress during the period when the knock knee is present. An interesting study done by Le Damany[5] on the present incidence of "tibial torsion" in comparison with its incidence in prehistoric skeletons, does not show any significant difference. This was taken to indicate that the wearing of shoes has not been a factor in the production of tibial torsion. No such study has been done on knock knee.

Leg irons and in particular, night splints have been devised to produce correction of knock knee in childhood. The use of such devices has usually been based on the presumption that treatment will be necessary.

It is evident that these 7 cases are not sufficiently large series to be statistically significant. They do however, constitute all the cases of knock knee without demonstrable underlying or contributing disease available from our files in which adequate follow-up examination, both clinical and radiologic, could be obtained. This experience is consistent with clinical studies of large groups of normal school children[3] in which the incidence of knock knee was found to be high at age $3\frac{1}{2}$ and to diminish and almost disappear by age 6. The large scale clinical studies previously done have not included follow-up examinations of the individual child, and in particular, have not included adequate radiologic documentation.

Although we have not yet encountered a case of physiologic knock knee in childhood which did not undergo spontaneous correction, there is some evidence that such cases do exist. Unfortunately, they are available as yet only from statistical studies without individual case histories and x-rays, or from impressions derived from experience, stated but not proven. Part of the purpose of the present communication is to suggest that if such cases are encountered, they should be fully documented and published. A comparison could then be made between those cases which disappear spontaneously and those infrequent cases which do not. In this way, criteria for differentiature might be established.

The frequent mention of rickets as a cause, or in fact the cause, of knock knee in childhood is of interest in the older literature. More recently, it has been pointed out that rickets is not the cause of this variation in lower extremity alignment in most cases. Rickets is included in Table I for the sake of completeness, but in fact, we have not been able to find a single case from our own files of vitamin D deficient rickets as a cause of knock knee in childhood. Vitamin D resistant rickets however, can and does occasionally cause knock knee, and other metabolic abnormalities associated with rachitic changes in bones (such as the de Toni Fanconi syndrome), can presumably also produce valgus deformity of the lower extremity.

It is of considerable importance in both the clinical and the radiologic assessment of knock knee that the standard position with the knees in contact be used. This has not been done consistently in our cases, and constitutes a weakness of the present report. We now use the standard anatomical position routinely in x-raying these children.

There has been little or no assessment, in published reports of knock knee in childhood, of the significance of asymmetry of the valgus deformity in the two lower extremities. Is the prognosis affected if one side is worse than the other? Three out of our seven cases had evident asymmetry of the alignment, and in one (Case #2) it was marked. Though not statistically significant, the return to normal alignment of these three suggests that the outcome is not affected by asymmetry.

The bone, joint, soft tissue and neurologic lesions which may cause knock knee other than of the physiologic type are listed in Table I. The differential diagnosis of these abnormalities from physiologic knock knee should, we believe, be evident from the clinical and radiologic findings.

TABLE I

Classification of Knock Knee
(adapted from Stelling and Meyer).

I. Physiological.
II. Pathological.
  A. Ligamentous abnormalities.
    1. Congenital absence or laxity
    2. Injury
  B. Torsional or angular changes of the femur or tibia, or both.
    1. Congenital developmental defect.
      a. hypophosphatasia
      b. osteochondromatosis
    2. Vitamin deficiency
      a. rickets
      b. vitamin D resistant rickets
    3. Disease
      a. Fanconi syndrome
      b. renal rickets
      c. chondro-osseous dysplasia
      d. chondro-ectodermal dysplasia
      e. fibrous dysplasia
      f. tarso-epiphyseal aclasia
      g. osteomyelitis
      h. osteoid osteoma
      i. familial metaphyseal dysplasia
    4. Injury
      a. trauma to the epiphyses
      b. trauma to the shaft
      c. surgical trauma
      d. x-ray therapy
    5. Paralytic.

Summary

Children from the ages of 2 years to 5 years show a tendency to develop bilateral knock knee, sometimes asymmetric. Previous investigations have shown statistically that this diminishes with further growth.

The present investigation shows that in seven individual cases, when the clinical and radiologic examination showed knock knee and no other abnormality affecting the lower extremities, the apparent deformity corrected spontaneously even though sufficiently severe to cause, in at least one case, definite interference with gait.

Although we have not yet encountered a case of physiologic knock knee which did not correct spontaneously, such cases if found, should be published in detail, in order to permit a comparison with the great majority which return to normal.

Acknowledgment

Case #6 was referred by Drs. T. A. Cowan and J. M. McIntyre, and Case #7 by Dr. J. M. McIntyre. Their help in supplying relevant clinical information is gratefully acknowledged.

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MEETING

9th International Congress of Radiology

The 9th International Congress of Radiology will take place in Munich, Germany, July 23rd - 30th, 1959. All enquiries should be addressed to: Professor Dr. H. v. Braunbehrens, Reitmorstrasse 29, Munich 22, Germany. No applications for registrations will be accepted after June 1, 1959.

There are still a few copies of the Preliminary Programme for the Congress available upon request to Central Office of the Canadian Association of Radiologists.

OSTEOMAS OF THE SKULL

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G. P. LARINI, M.D.
Herbert Reddy Memorial Hospital, Montreal

The incidence of osteomas is about 1% of all cranial and intracranial neoplasms.[1] They may be located anywhere in the cranium but are usually in the fronto-ethmoidal and orbito-ethmoidal sinuses. They may occur in the vault but are relatively uncommon there, the incidence being about 20% of all osteomas.

According to the commonest theory, these tumours originate from the embryonal type of osteoplastic cells that remain in the skull during developement. On the other hand, Fetissof[2] believes they originate through metaplasia of fibrous connective tissue, while in other cases the osteoma makes its appearance following local trauma. Their borders are not always sharply defined and sometimes, histologically, islands of fibrous dysplasia can be seen mixed with osteomatous tissue in the same lesion. This would tend to confirm the view of Smith and Zavaleta[3] that the osteoma is the end result of an ossifying fibroma.

Some pathologists doubt the neoplastic nature of the osteomas. Nevertheless, they may be considered as benign growths, growing very slowly and usually appearing before thirty years of age. Commonly, osteomas are formed near suture lines arising either from the surface of the bone (ivory type) or from the diploe (spongy type). Much less frequently they may arise within the cranium. Osteomas are asymptomatic and discovered accidentally even though they may reach a huge size. Cephalalgia is not a common complaint. No therapy is indicated unless for cosmetic reasons. Periodic follow-up is all that is needed. Sudden growth can occur following trauma or at puberty, withouth apparent reason.[4]

Courville and Crockett[5] have described the appearance of increased bone density following trauma, calling it, hyperostosing osteoma. No malignant changes have been described.

Case Reports

Of 10 osteomas of the skull which we have followed, 6 were in women, and 4 in men, as opposed to the usual prevalence in men, according to world literature. The average age was 25 years. Six were of the ivory type, four spongy, and in five cases the lesion was located in the occipital bone. Only three complained of mild headache, and in two of these, it disappeared after surgical removal was done for cosmetic reasons.

Diagnosis

Ivory osteoma may be round or oval in shape, showing markedly increased density with sharply defined borders. (Figs. 1, 2, 3).

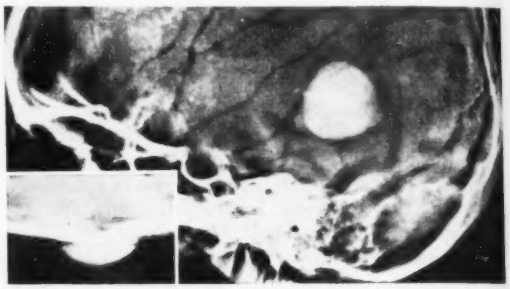

Figure 1.

They could either be flat as a plaque, or may be seen arising from the surface of the bone as a dome. In tangential views, it is sometimes possible to observe a pedunculum. Radiological diagnosis offers no difficulty, because they can easily be differentiated from tumoral hyperostosis, in many instances, because of clear-cut borders and homogenous structure.

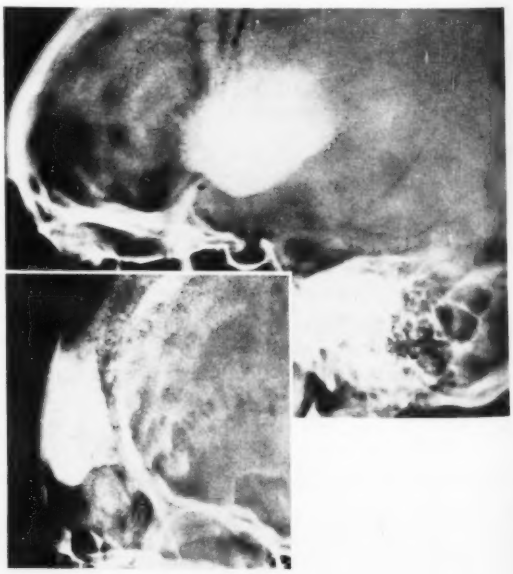

Figure 2.

Surrounding the osteomas there is no area of increased vascularity, and no alteration in the size of the vascular grooves. On the other hand, the spongy type differs in that they are situated within the bony structure, the diploe, and they may attain a huge size. Like the ivory type they also are well defined. Because of their location, the inner and outer tables separate and become thinner (Figs. 4, 5) but even when reduced to the thinnest degree

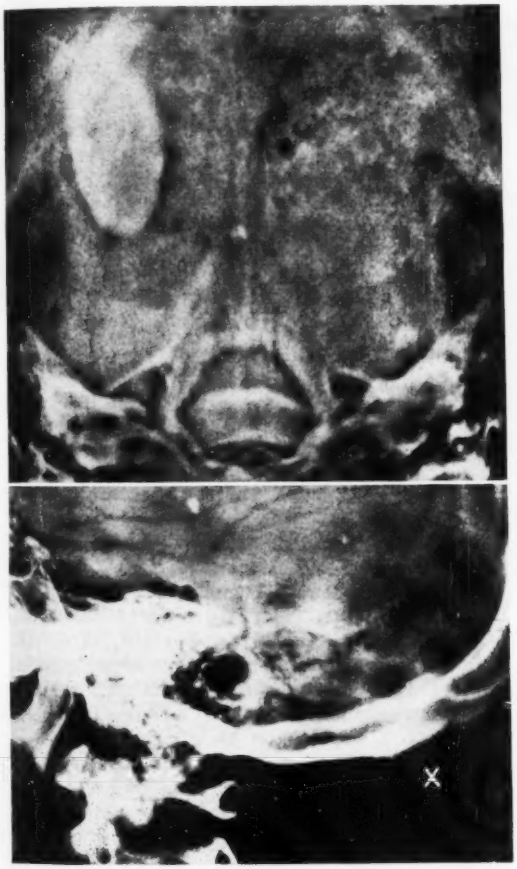

Figure 3.

possible, the inner table offers its greatest resistance to the invasion of the tumour. This type of osteoma presents a regular uniform diploic pattern (Fig. 4), but when they reach a huge size of long-standing, they may show degenerative changes appearing as irregularly distributed areas of alternating increasing and decreasing density.

An unusual finding in one of the cases was the observation of two arterial grooves converging towards the neoplasma. (Fig. 4.)

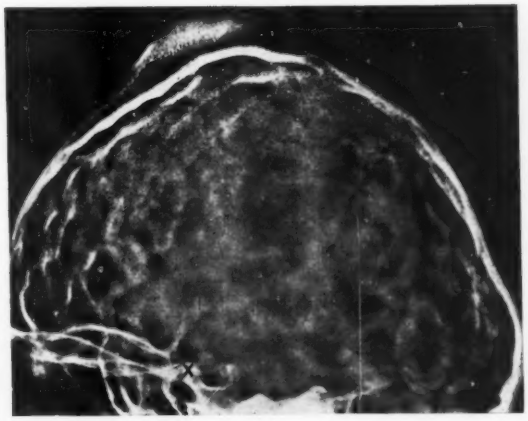

Figure 4.

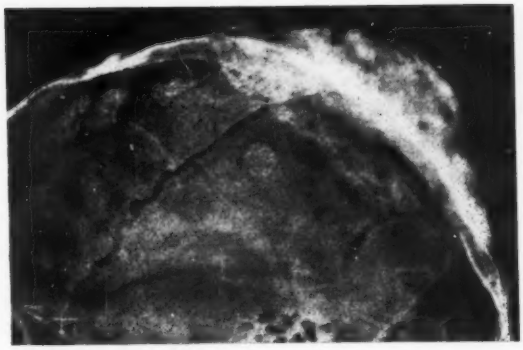

Figure 5.

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"EXPERIENCES WITH A NEW CONTACT LAXATIVE IN THE PREPARATION OF THE COLON FOR RADIOLOGICAL EXAMINATION"*

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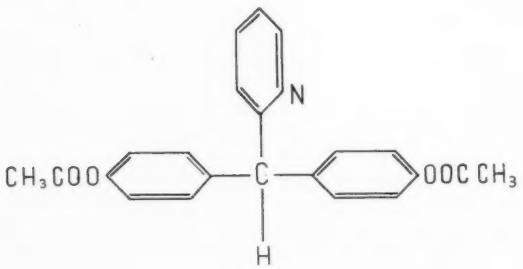
During the past few years there has been developed in Europe a new non-toxic "contact" laxative which has been reported to be uniformly efficient in action, easy to administer, and possessed of few undesirable side effects. This compound has recently been made available in this country under the trade name DULCOLAX†. On the strength of favourable reports which have appeared in the German literature over the past four years, one hundred and forty-two indoor and outdoor patients in the Royal Victoria Hospital have been prepared with this new substance during the past six months in an attempt to evaluate its efficiency as a colon evacuant prior to radiological examination.

Chemistry

A "contact" laxative is defined as a substance which acts direcly on the mucosa of the bowel to stimulate peristalsis, there being no absorption and therefore no action via the systemic circulation. Dulcolax is one of a group of contact laxatives made up of Bis (ρ-acetoxyphenyl)-2 pyridylmethane, and is the most active of this group of compounds due to the presence of a nitrogen atom in the alpha position on the pyridine ring:



Dulcolax is tasteless, odorless and colourless. It is insoluble in water and alkaline solution, but soluble in dilute mineral acids and organic solvents.

Pharmacology

Perfusion experiments have shown that the compound acts almost entirely upon the mucosa of the large bowel. Schmidt,[9] perfusing isolated segments of jejunum and ileum, has shown that the small intestinal mucosa is practically insensitive as demonstrated by the absence of increased motor activity; in similarly isolated segments of colon, marked increase in peristaltic activity was observed. That it is a true contact laxative, not acting by absorption, has been demonstrated by tying off the small intestine of experimental animals, and then administering a large oral dose; no stimulation of the colon was seen to occur[9]. Its contact nature has also been fairly conclusively demonstrated by Going and Schaumann[4] who were able to abolish the action of Dulcolax suppositories by anaesthetizing the mucosa of the rectum and sigmoid with topical anaesthetics. In addition, Schmidt[9] has shown that the subcutaneous dose required to produce a laxative effect is eight times the oral dose, the reverse of what would be expected if it acted by absorption and via the systemic circulation. Genz and Zindler[3] and Meyer-Burgdorff and Eichler[7] have demonstrated that the level of intestinal tone does not appreciably affect the action of Dulcolax suppositories, colonic peristalsis being stimulated in the presence of partial paralytic ileus and other conditions of lowered tone. In fact, Hobbs[6] has reported the satisfactory evacuation of a large amount of feces in a patient with megacolon refractory to other laxatives, and we have had the same experience with one patient.

While the exact mode of action physiologically is not yet completely understood, evidence is accumulating[10] that it may act by neurogenic stimulation through a local reflex arc. Considerable work is being done to further elucidate this mode of action.[10]

Toxicity has been shown repeateadly to be negligible. The therapeutic index is 1:200, and repeated clinical tests have shown no undesirable systemic effects on either the blood picture, or on hepatic or renal function. No effect has been observed on the pregnant uterus. The LD_{50} could not be determined orally since it has been impossible to kill experimental animals with Dulcolax.[9]

The materials used in this Study were supplied by Geigy Pharmaceuticals, Division of Geigy (Canada) Ltd.

†*Registered trade mark.*

Method of administration

Dulcolax is supplied in five mgm. enteric coated tablets, and ten mgm. suppositories. Numerous reports have stated that a single bowel movement generally occurs fifteen to forty-five minutes after insertion of a suppository, and approximately six hours after ingestion of tablets. The method of administration originally recommended was to insert one suppository the evening before examination to produce evacuation of the distal colon, two tablets at bed time to produce an effect the following morning, and a final suppository approximately one-half hour before radiological examination. In the present study, various combinations of suppositories and tablets have been used in an attempt to find the minimal dose necessary for complete evacuation, and some variation of the above recommended dosage has been found to be most efficacious in the majority of patients. Trials have been made using two, three and four tablets with p.m. and a.m. suppositories, although as yet the number of patients receiving four tablets is small.

A total of one hundred and forty-two patients have been prepared with Dulcolax alone and one hundred with castor oil and cleansing enemas, all prior to barium contrast examination of the colon. Most patients have had a low residue supper the evening before, and breakfast withheld the morning of examination. Each patient was evaluated from the points of view of thoroughness of cleansing of the large bowel (both feces and gas), completeness of evacuation of injected barium, and the side effects of the preparation.

Results

The results of the four techniques of preparation are shown in the accompanying table. It will be seen that of the one hundred and forty-two patients prepared with Dulcolax, a significantly higher percentage (54%) had "excellent" preparation than in the castor oil group (39%), although the totals of "excellent" and "adequate" preparations do not differ to any extent in the two groups. The completeness of evacuation of injected barium seemed to have no dependence on the technique of preparation. It is noteworthy however that in a number of patients prepared with castor oil, residual fluid in the colon from the cleansing enema was considered troublesome by the examining radiologist. This annoyance was seldom observed in the Dulcolax group, since cleansing enemas were not required.

The incidence of distressing side effects complained of by patients prepared by the two techniques showed a remarkable difference however. The majority of patients receiving the castor oil preparation complained of abdominal cramps and diarrhoea of varying degrees of severity. Only an occasional patient did not find this method of preparation distressing. While the results of the castor oil method are generally good, it should be mentioned that these figures hardly reflect the state of preparation seen in the department as a general rule. Special care was taken in this study to assure that all patients followed directions carefully, a condition most difficult to enforce in daily practice.

While many of the patients receiving Dulcolax stated on questioning that they had had a few cramps after one or both suppositories, these cramps were seldom very distressing. Cramps rarely occurred from the pills alone so that sleep was seldom interfered with the night before. There was practically no diarrhoea, even with four tablets, stools generally being soft but wellformed. No straining or tenesmus was complained of, nor were allergic or other undesirable side effects observed. Those patients who had had both methods of preparation at some time in the past were unanimous in their opinion that the contact laxative was distinctly less distressing. Not only were side effects less, but the attraction of being able to dispense with cleansing enemas was particularly gratifying to most. In this regard, many favourable comments have been made by the nursing staff of the hospital with respect to the saving of time brought about by absence of necessity for cleansing enemas on the wards.

Of the patients prepared with a suppository one-half hour before the barium enema, a number stated that they had not had a bowel movement before the examination was begun. For this reason, the time interval between this suppository and the examination was increased to two hours. Out of sixty-two patients who were questioned after this change was made, fifty-nine had had a bowel movement during the two hour interval.

We have found no relationship between the age of the patient and the degree of inadequacy of preparation, nor have results been better in ambulatory than in bed-ridden patients. These facts appear to substantiate previous evidence that the action of Dulcolax is independant of colonic tone. In addition, Aue[1] concluded in a study of the use of

Dulcolax in children that no untoward subjective or objective side-effects occurred with dosages commonly recommended for adults.

The majority of patients in whom preparation was described as "adequate" showed small amounts of feces and gas in the caecum and ascending colon, due probably to emptying of the distal small bowel coincident with colonic peristalsis stimulated by the last suppository. This aspect of the problem has been particularly troublesome in those patients in whom double contrast examination has been necessary, and for this reason one and a half ounces of castor oil has recently been added to the four tablet Dulcolax preparation in order to produce complete cleansing of the small bowel as well as the large bowel. As expected, this method has been found to be efficacious in almost all patients on whom it has been used. It is quite conceivable that a greater number of tablets than four would clean the proximal colon more completely, and tests with higher dosages are planned.

Despite the contact nature of Dulcolax as a laxative, irritation of the colonic mucosa is rare. Fluoroscopically we have noticed no increased irritability or spasm of any portions of the colon, although such effects following castor oil and cleansing enemas are well known to radiologists. By adding fifteen mgms. of Dulcolax to the injected barium suspension, Schlegel[8] observed prolonged peristalsis beginning in the distal ascending colon and progressing slowly to the sigmoid; no local spastic contractions were seen to occur. He recommends this technique as a means of procuring complete evacuation of injected barium for visualization of the mucosal pattern but as yet we have had no personal experience with the use of Dulcolax in this manner. That no direct irritation of colonic mucosa occurs has been demonstrated by Barth[2] and Hauff[5] who have reported no change in the sigmoid or rectal mucosa on sigmoidoscopic examination, even in patients who had received Dulcolax continuously over a ten-week period. We have examined six patients in this manner, and have observed a minor degree of mucosal hyperaemia in one only.

So far we have been unable to demonstrate any definite contra-indications to the use of Dulcolax, nor has any been reported in the literature.

Occasionally physicians have consulted us requesting advice as to means of cleaning out colons in which barium from previous upper gastro-intestinal examinations has become impacted. Dulcolax has been found to be often, but not invariably effective in these cases where standard methods of purgation have failed. In these stubborn cases, addition of Dulcolax to cleansing enema fluid might prove especially effective for ward use. Better still, it seems logical that the addition of Dulcolax to the barium suspension used in examination of the upper gastro-intestinal tract might well act as a preventative of fecal impaction, and trials with this technique are planned for the future.

Although it may be suggested that other variations of dosage than those prescribed might be equally as efficacious, we consider preparations two and three (see table) as minimal requirements for average use. The necessity for the evening tablets and morning suppository is unquestioned, but we are not

TABLE

Character of Bowel Preparation	Castor Oil + Cleansing Enema	DULCOLAX			
		I	II	III	Avge. %
	100 Patients	68 Patients	30 Patients	44 Patients	142 Patients
EXCELLENT	39%	47%	47%	68%	54%
ADEQUATE	57%	47%	50%	23%	40%
INADEQUATE	4%	6%	3%	9%	6%

Legend to Table:

"Excellent" — No feces or fluid in the large bowel; only minimal gas.
"Adequate" — Small amounts of feces, fluid or gas, but of insufficient quantity to interfere with diagnostic quality.
"Inadequate" — Too much feces or fluid for adequate evaluation, necessitating repeat examination.
Dulcolax I — One suppository and 2 tablets p.m.
One suppository half-hour before examination.
Dulcolax II — Same as I except a.m. suppository *2 hours* before examination.
Dulcolax III — Same as II except *three* tablets instead of two.

yet completely convinced of the need for the evening suppository in all patients. It will be seen from the table that of the three dosage schedules of Dulcolax tested, the last showed a higher percentage of "excellent" results than the first two, and this schedule is now being followed without exception.

Summary

1. One hundred and forty-two patients have been prepared for radiological examination of the colon with a new contact laxative (Dulcolax), and the results compared with a group of one hundred patients prepared with castor oil and cleansing enemas.
2. Both methods of preparation produced a high percentage of adequately cleansed colons, although the number of preparations classified as "excellent" was proportionately greater with the contact laxative.
3. The incidence of distressing side effects was significantly lower in those patients receiving the contact laxative. An analysis of acceptance of the two methods in those patients receiving both showed an almost unanimous preference for the contact method, not only because of less side effects but because of the lack of necessity for cleansing enemas.
4. Toxicity of the drug has been found to be negligible and no contra-indications to its use have been recorded. It is believed that its effectiveness and ease of administration will result in a significant reduction in the load on nursing care of hospital patients.

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10. Personal Communication.

MEETING

Section of Radiology (Canadian) C.M.A./B.M.A. Edinburgh Meeting — July 18th to 25th, 1959

The scientific program for the Canadian Section of Radiology for the above meeting in Edinburgh is as follows:

COBALT^{60} IN THE TREATMENT OF ORAL CANCER
Dr. Ivan H. Smith, London

COBALT^{60} IN THE TREATMENT OF ORAL CANCER
Dr. T. A. Watson, Saskatoon

HYPERPLASTIC CHOLECYSTOSES AND THEIR CHOLECYSTOGRAPHIC MANIFESTATIONS
Dr. Albert Jutras, Montreal

THE FACIAL SMASH
Dr. E. F. Crutchlow, Montreal

Number of Sessions — 2.

REQUIREMENTS FOR THE CLINICAL USES OF RADIOACTIVE ISOTOPES*

F. D. SOWBY, M.D.
Radiation Services
Department of National Health and Welfare
Ottawa, Ontario

Radioisotopes were made available for many purposes after the end of World War II. In Canada, isotopes were supplied by the National Research Council's atomic energy project at Chalk River, and in 1946 a clinical subcommittee was established by the National Research Council to deal with the diagnostic and therapeutic uses of radioactive material. From the beginning the subcommittee established the principal that radioisotopes should be available only to properly qualified institutions or individuals. This subcommittee functioned from 1946 until 1952, and during that time it reviewed all applications for clinical uses of radioisotopes.

In 1952, following the establishment of Atomic Energy of Canada Limited as a crown company, the National Research Council subcommittee was replaced by the Atomic Energy of Canada Limited Advisory Committee on the Clinical Uses of Radioisotopes; the membership of the committee remained essentially the same. Through this Advisory Committee, Atomic Energy of Canada Limited advised the Atomic Energy Control Board on the clinical uses of radioisotopes. (The Atomic Energy Control Board is the statutory body charged with the responsibility of carrying out the provisions of the Atomic Energy Control Act.)

In 1955 the Department of National Health & Welfare accepted the responsibility of advising the Atomic Energy Control Board on the clinical uses of radioisotopes, in addition to its previous function of acting as the Board's adviser on the health aspects of the other uses of radioactive materials. To assist it in assessing clinical applications, the Department has formed its own Advisory Committee, consisting of essentially the same members as the previous committee. The Committee is representative of expert experience in the clinical uses of radioactive isotopes; within the Advisory Committee there is an Executive Council, which carries out the policy set by the Advisory Committee.

The policy of the Committee is based on the policies of the previous committees of the National Research Council and Atomic Energy of Canada Limited. In general it is the Committee's policy to encourage the proper use of radioisotopes in humans, to ensure that adequate facilities and experience are available, and to discourage uses that may be hazardous to the patient or to others. The Committee has made certain recommendations and requirements which conform with practice and experience elsewhere. These are based on the principal that when radioisotopes are being used for diagnostic or therapeutic purposes, the dose should be kept as low as is consistent with medical necessity. Because of the greater hazard involved, the use of radioisotopes in children and pregnant women is discouraged unless there is a compelling reason.

Let us take the case of hypothetical physician who wishes to use isotopes for clinical purposes and see what he must do to obtain the material. He first of all submits an application to the Commercial Products Division of Atomic Energy of Canada Limited, and gives details of the proposed use. The application is forwarded to the Department of National Health and Welfare where first of all his physical facilities such as the isotope laboratory, safety equipment, measuring instruments and so on are reviewed in terms of radiation protection. Then the application is forwarded to the Advisory Committee on the Clinical Uses of Radioisotopes, which considers the proposal in terms of the general policy outlined above. The application must come from an institution where the isotope program is under the guidance of a local isotope committee, whose membership consists of physicians trained in internal medicine, haematology and radiology, and, where possible, a radiation physicist. The applying physician must have had previous training and experience in the physical aspects of radiation such as basic radiobiology, radioactivity measurement and instrumentation, monitoring techniques, and methods for the safe handling of radioisotopes. He must also have had training and experience in the actual assessment of patients for isotope administration, the measurement and administration of the doses, the making of radioactivity measurements and plotting of data, and the follow-up of patients through the treatment and post-treatment periods. The time spent in this training should be not less than the equivalent of two months full-time work.

Presented at Annual Meeting, The Canadian Association of Radiologists, January 12-15, 1958 London.

The physician is asked to obtain a letter of recommendation from the person under whom he took this training.

If the isotope in question is a sealed gamma-ray source the responsible user must be a certified radiotherapist, and in the case of a teletherapy unit there must be a radiation physicist available for full-time consultation. The user of beta-ray applicators must be a specialist in therapeutic radiology, ophthalmology, or dermatology with relevant experience in the use of beta-rays or soft X-rays in the treatment of superficial lesions.

The Committee has made specific recommendations for some of the more commonly used isotopes such as I^{131}, P^{32}, and Au^{198}. For example, the routine diagnostic dose of I^{131} should not exceed 25 microcuries, and with scintillation techniques it can often be much less. ~~should have participated in the treatment of~~ diseases of the blood should be under the supervision of a physician trained in internal medicine, haematology or therapeutic radiology.

The intracavitary or interstitial use of P^{32} in the treatment of cancer should be supervised by a therapeutic radiologist, and where surgical assistance is required the surgeon should have participated in the treatment of patients by this method. The use of P^{32} for the localisation of tumours such as those of the brain and the eye requires a broad experience in the use of radioisotopes and in the diseases being studied.

Au^{198} is of use as an intracavitary injection for the palliative treatment of cancer, and in the direct treatment of certain tumours. Because the quantities handled are relatively large, the user should have had special training in the specific uses proposed, or in closely related treatments such as the interstitial use of radium.

The experimental or non-routine use of radioisotopes in human subjects, whether for research, diagnostic or therapeutic purposes is limited to physicians with broad radioisotope experience. Proposals for the experimental use of radioisotopes must be supported with a detailed proposal, which should preferably have been preceded by studies in animals aimed at establishing assimilation, distribution, selective localization and excretion of the radioisotope in question sufficiently well to permit extrapolation to man for dosage purposes. Ordinarily radioisotopes with half lives greater than 30 days are not available for internal use in humans unless prior animal studies have established the metabolic properties noted above. It is recognised however, that special circumstances may arise which indicate the desirability or necessity for the use of long-lived isotopes where prior animal data are not available. Such proposals should be limited to patients suffering from diseases of such a nature that there is no reasonable probability of the radioactivity employed producing manifest injury.

The use of radioisotopes in normal subjects for experimental purposes is limited to volunteers to whom the intent of the study and the effects of radiation have been explained and who are unlikely to be exposed to significant additional amounts of radiation. The use of radioisotopes for experimental purposes normally excludes infants, pregnant women and volunteers for a long series of studies.

Patients containing more than 30 mc. of a gamma-emitting isotope are required to be kept in hospital in order to prevent exposure of his family and the general public. To protect other patients and hospital staff precautions should be taken concerning isolation of the patient, shielding, monitoring and disposal of excreta. Precautions should also be taken to ensure that cadavers containing radioisotopes cannot be hazardous to pathologists, under-takers and others.

The requirements that have been discussed refer to the use of isotopes in institutional use. In individual practice outside an institution certain well-established diagnostic uses of radioiodine and radiophosphorus may be permitted. Physicians applying to use these isotopes in individual practice must have had extensive training and experience in the clinical uses of radioisotopes.

This outline of the requirements for the clinical uses of radioisotopes has been kept general and short. Further details are found in the Policy of the Advisory Committee on the Clinical Uses of Radioisotopes, and in a pamphlet called, Laboratory Facilities for Handling Radioisotopes; both of these can be obtained from Radiation Services, Department of National Health & Welfare, Ottawa.